The Effects of Vitamin A Supplementation on the Morbidity of Children Born to HIV-Infected Women

ABSTRACT

Objective. The effects of vitamin A supplementation on morbidity of children born to human immunodeficiency virus (HIV)-infected women were evaluated in a population where vitamin A deficiency is not endemic.

Methods. A randomized, placebo-controlled trial of vitamin A supplementation was carried out in 118 offspring of HIV-infected women in Durban, South Africa. Those assigned to receive a supplement were given 50 000 IU of vitamin A at 1 and 3 months of age; 100 000 IU at 6 and 9 months; and 200 000 IU at 12 and 15 months. Morbidity in the past month was then recalled at each follow-up visit. Analysis was based on 806 child-months.

Results. Among all children, the supplemented group had lower overall morbidity than the placebo group (OR = 0.69; 95% confidence interval [CI] = 0.48, 0.99). Among the 85 children of known HIV status (28 infected, 57 uninfected), morbidity associated with diarrhea was significantly reduced in the supplemented infected children (OR = 0.51; 95% CI = 0.27, 0.99), whereas no effect of supplementation on diarrheal morbidity was noted among the uninfected children.

Conclusion. In a population not generally vitamin A deficient, vitamin A supplementation for children of HIV-infected women appeared to be beneficial, reducing morbidity. The benefit was observed particularly for diarrhea among HIV-infected children. (*Am J Public Health.* 1995;85:1076–1081)

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Introduction

This article reports a test of the hypothesis that vitamin A supplementation for children of human immunodeficiency virus (HIV)-infected women will reduce morbidity even in a population where vitamin A deficiency is not endemic.

Administration of vitamin A to children with overt and marginal vitamin A deficiency has been shown to reduce mortality.[1,2] Morbidity in infants and children has also been reduced, although less consistently.[3] In one African example, in Ghana,[4] a country with borderline vitamin A deficiency by World Health Organization criteria, those infants receiving supplements had fewer hospital admissions and clinic attendances, although total episodes of diarrhea and acute respiratory infections were not significantly reduced. In Brazil, vitamin A supplementation reduced the prevalence of severe diarrhea when the supplemented and placebo groups of children were compared.[5]

In two controlled trials of vitamin A in measles (one, like the present trial, conducted in Durban, South Africa), morbidity and mortality were reduced with supplementation, even though neither study population was initially vitamin A deficient.[6,7] Measles infection may result in a depletion of vitamin A reserves, which can be remedied with supplementation. Supplementation strengthens humoral immune responses and increases numbers of lymphocytes.[8]

It therefore seemed reasonable to propose a trial of vitamin A supplementation for children born to HIV-infected women, also in Durban, South Africa. These children might be vitamin A deficient at birth because of vitamin A deficiency in the mother, or infected children might develop vitamin A deficiency associated with their own HIV infection. On the assumption that strengthening immune responses could be beneficial, intravenous administration of immunoglobulin has been investigated in the United States as a therapeutic intervention in HIV-infected infants in the hope of improving resistance to other infections.[9] Developing countries are unlikely to encourage the use of intravenous immunoglobulin, given the costs and logistics of its use, nor are they likely to be able to afford antiretroviral drugs such as zidovudine. Vitamin A supplementation, on the other hand, would be inexpensive and simple to administer, might strengthen immune responses, might reduce the severity of infectious-disease episodes, and perhaps prolong life.

In this article, we describe the methods and results of a double-blind, randomized, controlled trial of vitamin A supplementation for children born to HIV-infected women in Durban, South Africa.

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Editor's Note. See related editorial by Martorell and Ramakrishnan (p 1049) in this issue.

Subjects and Methods

Subjects

Subjects were recruited from among HIV-infected women who had attended the prenatal clinic and who delivered infants at King Edward VIII Hospital, Durban, from April 1991 through November 1993. The hospital, a long-established teaching unit of Natal University, has a large prenatal care service and maternity unit, with about 15 000 deliveries per annum. Most of the patients are Zulu, and many are referred to the hospital from peripheral and rural clinics. For this study, only women living within 10 miles of the hospital were included. Eligible mothers in the trial all had attended the prenatal clinic, and after pretest counseling, all had chosen to be tested for HIV (all but 5% of the prenatal attendees agree to testing). At that time, about 10% of all women tested through the clinic were HIV positive. The study was approved by the Ethics Committee, Faculty of Medicine, University of Natal. All women gave their written informed consent to participate in the trial.

At delivery, all mothers recruited into a related study of maternal–infant HIV transmission who had, over the period of this study, delivered full-term infants were asked to attend a follow-up clinic after 1 month. The 118 mothers who did so were invited to take part in the vitamin A intervention trial. All accepted and joined the trial. (This high acceptance rate is the usual experience in the department. The promise of medical supervision is highly valued by the mothers.) Preterm infants, often given vitamin A routinely, were not included in the trial.

For lack of statistical power, a study of the effects on mortality was never contemplated. We calculated, however, that a sample size of 120 had sufficient power to detect a reduction in morbidity from 50% to less than 25%. In practice, the analytic method applied here permits every visit to be used in the analysis, and it accretes greater statistical power than initially calculated for individuals in the sample.

Follow-Up

Mothers were asked to attend a follow-up clinic when their infants reached 2 months and 3 months of age and thereafter at 3-month intervals up to 18 months on days prespecified by the protocol. Mothers were also encouraged to attend the clinic during the intervening period if they had problems. Their traveling costs were reimbursed, and home visits were made to follow-up defaulters.

Measurement of Morbidity

The morbidity data reported here reflect the current condition of the child at each scheduled clinic visit and a 1-month morbidity recall. The mother was given a card on which to record illnesses experienced by the child. At each scheduled clinic visit, the child received a full clinical examination, and all morbidity in the past month was recorded. The mother was closely questioned about any reported illness episode to ensure that it met the definition for each condition. The incidence, duration (more than 7 days), and severity (hospital admission) of the following were recorded: diarrhea (four or more loose watery stools a day); upper-respiratory-tract infection (presence of one or more of the following: rhinitis, throat infection, ear infection, or cough); lower-respiratory-tract infection (presence of cough with one or more of the following: rapid breathing, chest indrawing, crackles, or wheezing); isolated fever; thrush; and rash. Special attention was also paid to possible side effects arising from vitamin A treatment. Weight and height were recorded at 3-month intervals, with the National Center for Health Statistics growth charts as the reference standard.

Over 95% of the study infants were initially breast-fed. About half were exclusively breast-fed for 6 months. No significant differences in breast-feeding were found by treatment group.

Randomization and Treatment Regimen

Identifier numbers indicating vitamin A treatment or placebo were randomly allocated from a table of random numbers. All investigators and participants were blind as to the treatment group of the children. At 1 and 3 months the children received orally 50 000 IU of water-miscible vitamin A (retinyl palmitate, Arovit Drops, Roche, Basel, Switzerland) or an equal volume of placebo, and at 6 and 9 months they received a similar preparation of 100 000 IU of vitamin A or placebo. Both the placebo and vitamin A were administered in an amber-colored syringe that had been filled and appropriately numbered by the person holding the trial code. At 12 and 15 months, the children were given orally the contents of an amber-colored gelatin capsule containing either 200 000 IU of retinyl palmitate in arachis oil and 40 IU of vitamin E as an antioxidant (Roche, Basel, Switzerland) or a placebo with arachis oil and 20 IU of vitamin E. The capsules looked identical and were placed in number-coded envelopes from which they were removed when appropriate. In November 1993, after recruitment into the trial had been stopped, the vitamin A drops and capsules were analyzed for potency by the local Roche laboratory (Isando, South Africa), which was unaware of their contents. The mean concentration of the Arovit Drops was 142 500 IU/mL, which represents 95% potency, and the mean concentration of the capsules was 191 000 IU/capsule, which represents 95.5% potency.

TABLE 1—Numbers of Children Enrolled in Study, Mortality, HIV Status, and Follow-Up in Vitamin A and Placebo Groups

	Treatment Assignment	
	Vitamin A	Placebo
No. enrolled	60	58
No. deaths by end of study		
HIV infected	3	6
Infection status not established	2	0
No. alive		
HIV infected	10	9
Uninfected	27	30
Infection status not established	18	13
Total no. child-months of follow-up	416	390
% followed to		
6 mo	83	75
12 mo	64	67
18 mo	42	37
Based on total duration of follow-up:		
% children attending all treatment or placebo visits	96	98
% children attending every month until 18 mo	69	71

Diagnosis of HIV Infection in the Children

The diagnosis of HIV infection in the children was made on the basis of a

TABLE 2—Baseline Characteristics of Vitamin A and Placebo Groups: Sex, Maternal Age and Parity, Nutritional Parameters, and Morbidity

	Treatment Assignment		
	Vitamin A	Placebo	P[a]
% male	50.0	56.9	.453
Mean maternal age, (y)	25.0	24.8	.855
Mean parity	2.2	2.4	.379
Nutritional parameters			
% with weight for age below 2 standard deviations of the standard	0	3.4	.239
% with height for age below 2 standard deviations of the standard	6.7	5.2	1.000
Pretreatment morbidity,[b] %			
Diarrhea	6.7	5.2	1.000
Thrush	18.3	31.0	.109
Lower-respiratory-tract infection	8.3	1.7	.207
Upper-respiratory-tract infection	21.7	20.7	.897
Rash	3.3	8.8	.268

[a]*P* values were calculated with the chi-square test for categorical variables, except for comparisons with any cell sizes less than 5, in which case Fisher's exact test was used. The *t* test was used for continuous variables.
[b]At least one occurrence of the condition in the first month.

TABLE 3—Morbidity for All Infants in the Trial (Infected, Uninfected, and Status Not Established Combined): Vitamin A vs Placebo Groups

	Incidence Density per 100 Child-Months (No. Episodes)		
Morbidity	Vitamin A (n = 416 mo)	Placebo (n = 390 mo)	Model Odds Ratio (95% CI)
Diarrhea	19.7 (82)	25.6 (100)	0.71 (0.47, 1.08)
Diarrhea lasting ≥ 7 days	6.3 (26)	9.7 (38)	0.62 (0.32, 1.20)
Hospitalized for diarrhea	0.5 (2)	3.1 (8)	0.23 (0.04, 1.20)
Thrush	5.0 (21)	7.2 (28)	0.69 (0.37, 1.28)
Lower-respiratory-tract infection	7.7 (32)	11.0 (43)	0.67 (0.37, 1.21)
Hospitalized for lower-respiratory-tract infection	1.7 (7)	1.8 (7)	0.94 (0.32, 2.70)
Upper-respiratory-tract infection	40.1 (167)	46.7 (182)	0.77 (0.53, 1.10)
Rash	11.1 (46)	10.0 (39)	1.12 (0.63, 1.98)
All morbidity	36.5 (152)	45.4 (177)	0.69 (0.48, 0.99)

positive HIV antibody test at 15 months (enzyme-linked immunosorbent assay [ELISA], Abbott, N Chicago, Ill). Children who had lost maternal antibody by 15 months or sooner were diagnosed as uninfected. Among the 11 deaths in children younger than 15 months, 9 were diagnosed as HIV infected on the basis of criteria laid down at the Ghent workshop[10] (i.e., at least one HIV-related sign or symptom when last seen and death from severe infection or persistent diarrhea beyond the first 4 weeks of life). Infection status could not be established for the remaining two deaths, nor for 33 children lost to follow-up before 15 months of age who had neither lost antibody nor developed clinical disease when last seen. At the time the analysis reported here was undertaken, all surviving children were 15 months or older.

Vitamin A Concentrations

Vitamin A concentration was measured in a subsample of 36 infants, tested at 1 month and 9 months. These assays were to establish comparability of the supplemented and placebo groups at baseline and to validate the increase of vitamin A levels with supplementation. Sera were collected from alternate infants at baseline. Out of a necessary economy, the analysis was limited to the first 36 infants who had visited the clinic at 9 months and who had been tested at 1 month.

One milliliter of venous blood was obtained and centrifuged within 5 hours. The serum was separated and stored at −70°C until analysis. Precautions were taken to protect the serum from light during separation, storage, and analysis. Vitamin A (serum retinol) was measured by normal-phase high-pressure liquid chromatography with fluorescence detection. The method used was a modification of a previously reported method.[11] The instrument used was a Hewlett-Packard HP 1090, which was attached to a programmable fluorescence detector (HP 1046). The column was a normal-phase microbore column (Spherisorb S3W; Phase Sep, Queensferry, Wales, United Kingdom). The method was validated by using standard reference material for retinol (SRM 968a) from the National Institute of Standards and Technology (Gaithersburg, Md). The technician was blind to the treatment regimen.

Statistical Methods

In accord with the a priori hypothesis, the primary intention-to-treat analysis compared the supplemented and placebo groups overall with respect to all morbidity. The components were diarrhea, diarrhea lasting 7 or more days, thrush, lower- and upper-respiratory-tract infections, rash, and hospitalization for diarrhea and for lower-respiratory-tract infections. The occurrence of each condition separately and of all morbidity combined was expressed as incidence density morbidity rates. These were calculated by dividing the number of episodes of the condition (multiple episodes of the same condition in a single month were counted as one episode), and for all morbidity the number of months in which any of the conditions had occurred, by the child-months of observation.

Odds ratios (ORs) and standard errors to compare morbidity between groups were estimated from logistic regression models with repeated measurement that make use of generalized estimating equations. This method, which can take into account within-individual correlation, was specifically developed for the analysis of longitudinal data sets comprised of repeated observations of an

TABLE 4—Observed Morbidity Rates per 100 Child-Months of Follow-Up among Known HIV-Infected Children and Uninfected Children: Vitamin A vs Placebo

Morbidity	HIV Infected Children			Uninfected Children		
	Morbidity Rate (No. Episodes)		Treatment OR (95% CI[a])	Morbidity Rate (No. Episodes)		Treatment OR (95% CI[a])
	Vitamin A	Placebo		Vitamin A	Placebo	
Diarrhea	21.6 (21)	35.1 (34)	0.51 (0.27, 0.99)	21.1 (56)	23.1 (63)	0.89 (0.37, 2.10)
Diarrhea lasting ≥ 7 days	10.3 (10)	20.6 (20)	0.44 (0.17, 1.18)	5.7 (15)	6.6 (18)	0.84 (0.23, 3.13)
Hospitalized for diarrhea	2.1 (2)	8.3 (8)	0.23 (0.05, 1.19)	0	0	
Thrush	9.3 (9)	13.4 (13)	0.66 (0.25, 1.73)	3.4 (9)	4.4 (12)	0.77 (0.20, 2.94)
Lower-respiratory-tract infection	11.3 (11)	17.5 (17)	0.60 (0.29, 1.24)	6.4 (17)	8.5 (23)	0.75 (0.24, 2.38)
Hospitalized for lower-respiratory-tract infection	3.1 (3)	5.2 (5)	0.59 (0.13, 2.65)	1.1 (3)	0.7 (2)	1.57 (0.16, 15.9)
Upper-respiratory-tract infection	47.4 (46)	46.4 (45)	1.04 (0.48, 2.24)	38.5 (102)	45.1 (123)	0.76 (0.31, 1.87)
Rash	17.5 (17)	9.4 (9)	2.07 (0.61, 7.08)	8.7 (23)	10.3 (28)	0.83 (0.21, 3.35)
All morbidity	45.5 (46)	54.8 (51)	0.69 (0.36, 1.31)	44.6 (90)	52.1 (175)	0.74 (0.34, 1.61)
No. follow-up months	97	97		265	273	

Note. Children whose infection status was not established were excluded. Results were not different when these children were included either with the infected or the uninfected subgroup.

[a]Confidence intervals (CIs) for odds ratios (ORs) for the treatment effect were calculated from a multivariate model based on generalized estimating equations, specifying as the outcome the occurrence of the condition (1 or 0) and as the covariates treatment status (vitamin A [1] placebo [0]), HIV status (infected [1] uninfected [0]), and interaction between HIV status, treatment, and child's age (continuous).

outcome in the same individuals over time.[12–14] For the primary analysis, the logit transformation of the outcome (occurrence of each condition coded dichotomously as either absent or present) was modeled as a function of the treatment status (vitamin A or placebo). The independent working correlation structure and robust standard errors were used. Analyses were conducted with a macro written for SAS software by M. Rezaul Karim.[15]

A prespecified corollary to the primary hypothesis tested whether supplementation was particularly effective for HIV-infected infants. At the time and place this study was carried out, the diagnosis of HIV infection in the offspring of infected mothers had to rely on clinical features and the persistence of antibody to the age of 15 months. The necessary delay precluded randomization of HIV-infected infants at entry. Therefore, this question was examined by comparing treated and untreated children within infected and uninfected subgroups. Morbidity rates and odds ratios were calculated within the HIV status strata. Children whose infection status was not established were excluded (20 in the vitamin A group, 13 in the placebo group). To investigate the sensitivity of the analysis to the exclusion of children for whom HIV status was not established, further analyses were conducted in which children of unknown HIV status were either all included with the infected subgroup or all included with the uninfected subgroup.

Each condition was analyzed separately with multivariate logistic models based on generalized estimating equations. Odds ratios and confidence intervals (CIs) were determined for the effect of the treatment on HIV-infected and uninfected infants. Outcome was dichotomous, recorded as the presence (coded as 1) or absence (coded as 0) of the condition in the preceding month. Covariates were treatment status (supplemented [1] vs placebo [0]), HIV status (infected [1] vs uninfected [0]), and interaction between HIV status, and treatment, and the child's age (as a continuous covariate).

Results

Table 1. Of 118 children who entered in the trial, 11 died, all before 6 months of age: 5 of 60 in the supplemented group and 6 of 58 in the placebo group. (For two deaths in the supplemented group, the infection status could not be established.) In a life-table analysis, survival time did not differ by treatment. The numbers of HIV-infected children in the supplemented and placebo groups were similar (13 vs 15, respectively). The groups fared equally in terms of follow-up.

Table 2. Randomization produced comparable groups in terms of baseline characteristics at the 1-month visit, before randomization. No statistically significant differences by treatment assignment in sex, maternal age or parity, nutritional parameters, and reported morbidity in the previous month were observed. There were no significant differences (data not shown) between supplemented and placebo groups in terms of sociodemographic characteristics (education, previous sibling loss, availability of domestic water and electricity, and household crowding). These data were not available for the whole sample.

The vitamin A concentrations were examined by treatment status at 1 month and 9 months of age in the subsample of 36 infants selected as described in "Vitamin A Concentrations." At assignment, when the first vitamin A level was assessed, the treatment groups did not differ (mean concentrations of 29.6 μg/dL in the supplemented group and 27.7 μg/dL in the placebo group). As expected, however, at 9 months, the supplemented group had significantly higher levels of vitamin A than the placebo group (mean concentrations of 38.4 μg/dL and 30.0 μg/dL, respectively; $P < .001$).

Table 3. Overall morbidity was significantly lower among the children receiving supplementation (OR = 0.69; 95% CI =

0.48, 0.99). For almost every condition, assessed separately, rates with supplementation were lower, but the upper confidence limit was greater than 1. In the supplemented group, incidence was reduced for all diarrhea by 29%, for diarrhea lasting 7 or more days by 38%, and for hospital admissions for diarrhea by 77%. Smaller differences were seen for thrush and for respiratory infections. There were no differences in the frequency of rashes or in weight gain between the two groups. Mean weight gain from 1 to 9 months was 4.42 kg (95% CI = 4.15, 4.70) and 4.84 kg (95% CI = 4.37, 5.31) in the vitamin A group and the placebo group, respectively.

Table 4. Among HIV-infected children, the reduction associated with vitamin A supplementation (controlling for age) was estimated to be 49% for all diarrhea (a significant reduction; $P < .05$) and 56% for diarrhea lasting 7 or more days. For children known to be uninfected, effects of supplementation were smaller for all diarrhea and for severe diarrhea (the interaction term in the model is not statistically significant). For hospital admissions for diarrhea (all were among infected children), the estimated reduction with supplementation was 77%.

Separate analyses of morbidity occurring below 6 months of age, at 7 through 12 months, and at 13 through 18 months (data not shown) found similar effects of treatment across the age strata.

Discussion

The women attending the King Edward VIII Hospital maternity service are not, in general, a vitamin A–deficient population. Thus, it is notable, if not very surprising, that the offspring of HIV-infected women were not vitamin A deficient at 1 month of age. Nevertheless, in accord with the primary a priori hypothesis, this study suggests that in this population vitamin A administered orally to the offspring of HIV-infected women in regular moderate to high doses beginning at 1 month of age reduces morbidity, at least through the first 18 months of life covered by this trial. The magnitude of the reduction in overall morbidity appears to be quite substantial. For specific conditions, the effects are generally in the same direction but do not reach significance.

As anticipated with sample sizes calculated for a hypothesis of reduced morbidity, we were unable to show a reduction in mortality. Loss to follow-up was considerable. Given randomization, the strict maintenance of blinding of both investigators and participants throughout the study, and an analysis that included all participants in the denominators, however, the results are unlikely to overestimate the effect of vitamin A supplementation.

The second a priori hypothesis was that the reduction in morbidity associated with vitamin A supplementation would be particular to HIV-infected children. The multivariate analyses support the hypothesis in that the effect appears to be strengthened in such children. This result is more vulnerable than the result for the primary hypothesis because a diagnosis of HIV infection could not be established in the almost one third lost to death or follow-up before 15 months of age. Nevertheless, the results are unchanged whether those for whom an HIV diagnosis was not established are excluded, included with the infected subgroup, or included with the uninfected subgroup. Thus, among supplemented children, those infected had a significant reduction in episodes of diarrhea compared with children receiving placebo who were infected, whereas no comparable treatment effect was observed among the uninfected children.

Treatment and placebo groups had similar nutritional and health indicators at baseline. However, no interim measures of characteristics that may have influenced morbidity in the two groups are available, nor are there laboratory measures of HIV viral load or of immune status in the children in the trial. In this respect, the study is not proof against all confounders (i.e., we did not estimate conditional treatment effects with adjustment for these variables), nor can it illuminate biological processes. Nevertheless, given the initial randomization, unbiased exposure, unbiased observation of outcomes, and no exclusions after randomization, the results remain valid within the appropriate limits of the statistical tests (i.e., the unadjusted treatment effect estimates are unbiased estimates of the conditional parameters).

The findings are consistent with biological knowledge, although they are to some degree tentative because of relatively small numbers. Human immunodeficiency virus infection is accompanied by multiple nutritional deficiencies including vitamin A deficiency.[16,17] In HIV-infected adults, vitamin A deficiency has been found in association with immunoparesis, accelerated progression to the acquired immunodeficiency syndrome (AIDS), and reduction in life span.[18] Among offspring of HIV-infected women, vitamin A deficiency has been associated with increased infant and perinatal mortality.[19,20] Whether this increase results from increased transmission of the virus, from accelerated progress of the infection in the infants, or from other causes is still unclear.

The likely mechanisms through which vitamin A reduces morbidity are rehabilitation of mucosal integrity and boosting of the immune response.[21,22] Both these protective barriers are known to be breached in HIV infection. Specifically, a decline in the number of $CD4^+$ T lymphocytes[23] correlates with the risk and severity of HIV-related clinical syndromes.[24] In humans and experimental animals deficient in vitamin A, vitamin A therapy corrects abnormalities and enhances impaired cellular and humoral immunity. Vitamin A works both in prior nutritional deficiency states[25] and in deficiency states (diminished blood levels) caused by the body's excessive consumption of vitamin A during severe disease.[6,7]

Vitamin A supplementation plausibly has an effect on morbidity in cases of HIV infection similar to that in cases of measles.[6,7] Measles virus affects $CD4^+$ lymphocytes,[26] with lymphopenia being an important indicator of the severity of measles[27]; conversely, vitamin A supplementation increases lymphocyte numbers and antibody response.[8] Serum levels of vitamin A in this study were similar to those among measles patients in whom large doses improved their clinical condition.[28]

In this study, vitamin A supplementation, administered to full-term infants in the postnatal period, did appear to raise vitamin A levels. An alternative procedure might have been to supplement the mothers at delivery.[29]

Vitamin A supplementation appeared to reduce morbidity associated with diarrhea. Associations were stronger with increasing severity of the diarrhea. In keeping with results from other studies,[3,5] this finding suggests that benefits of supplementation are owed to reduced severity of illness, rather than reduced numbers of episodes of illness. In HIV-infected children, diarrhea is among the prime causes of morbidity[30] and use of health services and, in Africa, an important cause of death.[31] Although a notable consequence of protracted diarrhea in HIV-infected children is growth retardation, we detected no differences in weight gain and length between treated and placebo groups. Growth velocity determinations might be more revealing.

The dose and schedule regimens of vitamin A used here seem to have been appropriate and well tolerated. No unforeseen difficulties were experienced with its use. Side effects (vomiting and bulging fontanelle) were monitored by history and, when possible, by clinical examination.

A reasonable inference, which will need to be examined in subsequent trials, is that vitamin A is beneficial for HIV-infected children, even if begun postnatally and even in a population not normally vitamin A deficient. Vitamin A is inexpensive and can be expected to benefit infected children by reducing the incidence and severity of diarrhea and the burden on health services and, not least, by improving the quality of life for the children and their caretakers. □

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